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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/049,373	06/21/2002	Isao Ishida	051023-0115	3667

22428 7590 06/22/2005

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EXAMINER	
TON, THAIAN N	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 06/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/049,373	Applicant(s) ISHIDA ET AL.	
	Examiner Thaian N. Ton	Art Unit 1632	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 25 May 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,3-5,9 and 25*.
   Claim(s) withdrawn from consideration: *6 and 10-24*.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☐ Other: _____.

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Continuation of 11. does NOT place the application in condition for allowance because: The prior rejection of claims 1-5, 8, 9 and 25 under 112, 1st paragraph, for new matter, is withdrawn in view of Applicants' deletion of the term "trans-chromosomic non-human mammal".Further, the rejection of claim 25 is withdrawn with regard to new matter, because of Applicants' amendment to the claim. The prior rejection of claims 1-5 and 9, under 112 1st paragraph for written description (pp. 5-8 of the Office action mailed 2/25/05) is withdrawn, in view of Applicants' amendment to the claims, now reciting "mouse".

The prior rejection of claims 1, 3-5, 9 and 25 under 112, 1st paragraph, for enablement (pp. 8-13 of the Office action mailed 2/25/05) is maintained for reasons of record. Applicants' amendments to the claims fail to enable the claims. The amendments to the claims do not fall within what has been determined to be the enabled scope of the invention. Applicants argue that they have now amended the claims to recite a "P450 3A family" gene, and that the specification describes several 3A family genes and clusters. This is not found to be persuasive in view of the prior rejection; as stated previously, the art of producing transgenic animals is such that the resultant phenotype is unpredictable, thus, even though the specification details various genes that are in the mouse CYP3A family, there is no analysis with regard to the resulting phenotype of mice who harbor various fragments that express other family members, other than the human CYP3A4A gene (which is found to be the enabled scope). The specification fails to provide any guidance with regard to the production of other mice expressing other cytochrome P4504A family gene members, and one would not be able to rely upon the state of the art to predict the resultant phenotype. Applicants argue that, with regard to the breadth of the claims encompassing chimeric animals, determination of threshold levels of gene expression is not a primary concern for those who practice microcell fusion in the context of creating trans-chromosomic aniamls, because most researchers are satisfied that a mouse produced by microcell fusion is suitable for metabolism for metabolism studies if it simply tests positive for the expression of a heterologous P450 gene, and thus, the gene expression is not an essential aspect of the claimed invention. See p. 9 of Applicants' response. This is not persuasive. It is reiterated that the instant specification does not provide sufficient guidance with regard to how to use the claimed animals, because certain of the claims (see claim 25) require that the gene is induced by a compound that induces the expression of the P450gene. There is no teaching or guidance by the specification with regard to how many cells would have to have this fragment in order to practice the claimed invention, and further, how much expression of those cells would be sufficient to produce the effect of expression of CYP3A4 enzyme upon administration of the substrate. Applicants provide Yoshida, Tomizuka (1997) and Tomizuka (2000) to provide support for this. The references have been considered, but are not persuasive for reasons stated above, that the claims require the expression of CYP3A upon administration of the substrate, and the specification fails to provide sufficient guidance with regard to the breadth of P2503A gene family, and how many cells, and how much expression would be sufficient to produce this effect. Accordingly, the prior rejection of record is maintained.

The prior rejection of claims 1-5,8,9 and 25 under 112, 2nd paragraph, is withdrawn in view of the deletion of the temr "trans-chromosomic".

The prior rejections of claims 1-5, 8, 9 and 25 under 102 (b) as being anticipated by Li (Archives of Biochem) or Li (Biochem Biophy. Res.) is withdrawn in view of the claim amendments, which state that the human chromosome is not integrated in the mouse cell genome.